

Application No. 10/672,689  
Amdt. dated June 7, 2006  
Reply to Office Action of Feb. 7, 2006

### **REMARKS/ARGUMENTS**

Claims 1-4, 7, 9-19 and new claims 41-44 are pending in this Application. Claims 41-44 are based directly on claim 1 and have been added to further define the subject matter of the present invention and fall within the elected group currently under prosecution. Applicants have added the new claims, without prejudice or loss of equivalents, for the sake of furthering the prosecution and allowance of the immediate claims.

The new language in claim 41 is found in the specification, namely, paragraph [0010] and Figure 9. The new claims also find support throughout the specification, e.g., paragraphs [0009], [0013], [0072], [0073] and Figures 4, 5 and 10. These paragraphs and figures include the specific terminology "native structure and integrity" and include examples of nerve tissue as well as the comparison of the graft of the present invention with other transplant grafts made by either a freeze/thaw and/or Triton X-100 methods. The Office Action mailed on February 2, 2006, includes the following rejections:

1. Claims 14 is rejected under 35 U.S.C. § 112 first paragraph.
2. Claims 1-4, 7 and 9-19 are rejected under 35 U.S.C. § 112 second paragraph.
3. Claims 15-17 and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Livesey, et al.
4. Claims 15-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Dennis, et al.
5. Claims 15-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gulati, et al.
6. Claims 15-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by Tanagho, et al.
7. Claims 15-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by Atala.
8. Claims 1-3, 9-14 and 17 are rejected under 35 U.S.C. § 103.
9. Claims 4, 7 and 18 are rejected under 35 U.S.C. § 103.

Applicants respectfully address the basis for each of the Action's rejections below.

#### ***Claim Rejections – Claim 14 is rejected under 35 U.S.C. § 112.***

The Action rejects claim 14 based on new matter. The claim has been amended to include the phrase "two or more" which is more definite than the term "several." Applicants respectfully submit that the phrase "two or more" is definite and the specification is enabled to support claim 14 in the claims as originally filed and complies with 35 U.S.C. § 112. Applicants submit that "several" is defined by

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Merriam-Webster online dictionary as: "several a: more than one (*several* pleas) b: more than two but fewer than many (moved *several* inches)." As such, the specification satisfies the written description requirement under 35 U.S.C. § 112. For the reasons mentioned above, the Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 112.

***Claims 15-17 and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Livesey, et al.***

Applicants disagree with the Action's analysis of U.S. Patent No. 5,336,616 to Livesey, et al., ("Livesey"), which is said to disclose the claimed invention. Livesey does not anticipate claim 15-17 and 19 of the present invention. As regards new claims 41-44, Livesey does not disclose the limitations related to nerve tissue, structural integrity, the reduction in the immune response of the graft or the enhanced capacity for regeneration produced by the method described. As such, it simply can not anticipate.

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979). The product of claim 15-17 and 19 can only be defined by the process steps by which the product is made and the process steps impart distinctive structural characteristics to the final product.

The process steps of the present invention and Livesey are different and as a result the products defined by the processes are different. Livesey discloses a product that is made by a process using different chemical agents to produce a product that has different properties than the product of the present invention. For example, Livesey discloses a product that is made by incubating the tissue, drying the tissue and cyropreparing the tissue. That process is VERY different from the process of the present invention. The decellularization of Livesey includes chemical treatments, including incubation in certain salts, detergents or enzymes. Livesey specifically discloses:

Triton X-100 polyoxyethylene (20) sorbitan mono-oleate and polyoxyethylene (80) sorbitan mono-oleate (Tween 20 and 80), sodium deoxycholate, 3-[(3-chloramidopropyl)-dimethylamino]-1-propane-sulfonate, octyl-glucoside and sodium dodecyl sulfate (c.9, 11.41-52)

Livesey does not disclose sulfobetaines, nor does Livesey disclose sulfobetaines with an anionic surface-active detergent.

Although it is true that zwitterionic detergents may have broad characteristics in common the

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compositions of compounds dictate their properties. Zwitterionic detergents may share general or broad characteristics, but they are not interchangeable as their specific characteristics are different. As the skilled artisan knows, different compounds (e.g., CHAPS and SB-10, SB-16) have different properties (e.g., the critical micelle concentration value, solubility, amount of damage to protein structures, amount of myelin basic protein removed and so forth) and with different properties, the ability to decellularize tissue is different. As the degree of decellularization is different the product must be different. The different properties of the compounds used in Livesey result in different components being removed from that tissue, thus Livesey does not contain the same composition as the present invention. As the products do not have the same internal structures and extracellular matrix (ECM) components, the present invention and the product of Livesey cannot be identical.

Therefore, the process of the present invention imparts distinctive structural characteristics to the final product. Applicants respectfully submit that the Livesey fails to meet the standard of 35 U.S.C. § 102(b). As such, Livesey does not anticipate any of the claims of the present invention. Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §102(b).

***Claims 15-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Dennis, et al.***

The Action rejects claims 15-19 under 35 U.S.C. § 102(b) as anticipated by Dennis, et al., ("Dennis") (U.S. Patent No. 6,207,451), which is said to disclose the claimed invention. Applicants respectfully submit that the cited reference fails to meet the standard of 35 U.S.C. § 102(b).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979). The product of claim 15-19 can be defined by the process steps by which the product is made and the process steps impart distinctive structural characteristics to the final product. Applicants respectfully submit that Dennis fails to meet the standard of 35 U.S.C. § 102(b).

The process steps of the present invention and Dennis are different and as a result the products defined by the processes are different. Dennis teaches a product made by a process using mammalian muscle construct, which is developed *in vitro* from cells extracted from mammals. The construct is made outside a living body and in an artificial environment. Furthermore, the mammalian muscle construct includes anchors, the tissue is exposed to ultraviolet light, the tissue undergoes pre-incubation in a tube and a mechanical shaker bath is used to completely dissociate the tissue. Immediately upon complete tissue dissociation, the tubes are centrifuged and the supernatant is aspirated and cells are reconstituted.

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The resulting product of Dennis is extremely different than the native, acellular tissue replacement of the present invention.

The processes and products thereof are different, Dennis does not disclose a native, cell-free tissue replacement or the product thereof, by obtaining a tissue replacement soaking the tissue replacement in a solution having one or more sulfobetaines, washing the tissue replacement in one or more solutions of a buffered salt, extracting with an anionic surface-active detergent and washing the tissue replacement in one or more solutions of a buffered salt. Dennis and the present invention use very different processes and as a result impart distinctive structural characteristics to the respective final products. It is unclear how the native, acellular tissue replacement of the present invention and the artificially grown mammalian muscle cells that are exposure to ultraviolet light, mechanically shaken bath until complete dissociation and then reconstituted are the same identical product.

The process of the present invention imparts distinctive structural characteristics to the final product. Applicants respectfully submit that the Dennis fails to meet the standard of 35 U.S.C. § 102(b). As such Dennis does not anticipate any of the claims of the present invention. Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

***Claims 15-19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gulati, et al.***

The Action rejects claims 15-19 under 35 U.S.C. § 102(b) as anticipated by Gulati, et al., ("Gulati"), which is said to disclose the claimed invention. Applicants respectfully submit that the cited reference fails to meet the standard of 35 U.S.C. § 102(b).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979). The product of claim 15-19 can be defined by the process steps by which the product is made and the process steps impart distinctive structural characteristics to the final product.

The process steps of the present invention and Gulati are different and as a result the products defined by the processes are different. Gulati discloses a product that is made by a process of harvesting degenerated nerve cell and repeatedly freezing them in N<sub>2</sub> (I). This is clearly a harsh mechanical and thermal treatment that does not separate out the components. The nerve cell is then placed on a dish of cultured cells (see page 120, section 2.3). It is unclear how a single nerve cell on an *in vitro* tissue culture that is repeatedly

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frozen and thawed is the same as a native, cell-free tissue replacement.

Gulati does not disclose a tissue replacement made by soaking a tissue in a solution having one or more sulfobetaines, washing the tissue replacement in one or more solutions of a buffered salt, extracting with an anionic surface-active detergent and washing the tissue replacement in one or more solutions of a buffered salt. Gulati and the present invention are clearly different in processes and as such impart distinctive structural characteristics to the final product. Therefore, the product in Gulati and the product of the present invention are different, made by different process and possess different characteristics.

Therefore, the process of the present invention imparts distinctive structural characteristics to the final product. Applicants respectfully submit that the Gulati fails to meet the standard of 35 U.S.C. § 102(b). As such Gulati does not anticipate any of the claims of the present invention. Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

***Claims 15-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by Tanagho, et al.***

The Action rejects claims 15-19 under 35 U.S.C. § 102(b) as anticipated by Tanagho, et al., United States Patent Number 6,371,992 ("Tanagho"), which is said to disclose the claimed invention. Applicants respectfully submit that the cited reference fails to meet the standard of 35 U.S.C. § 102(e).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979). The product of claim 15-19 can only be defined by the process steps by which the product is made and the process steps impart distinctive structural characteristics to the final product.

The process steps of the present invention and Tanagho are different and as a result the products defined by the processes are different. Tanagho discloses a product that is made using chemical methods that include a sodium desoxycholate solution containing sodium azide to remove cell membranes and intracellular lipids from the intermediate matrix. Tanagho does not disclose a tissue replacement product obtained by a soaking an obtained tissue replacement in a solution having one or more sulfobetaines, washing the tissue replacement in one or more solutions of a buffered salt, extracting with an anionic surface-active detergent and washing the tissue replacement in one or more solutions of a buffered salt.

Components are not interchangeable as their specific characteristics are different. As the skilled artisan knows, different compounds (e.g., sodium desoxycholate solution and SB-10, SB-16) have

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different properties (e.g., the literature critical micelle concentration value, solubility, amount of damage to protein structures, amount of myelin basic protein removed and so forth) and with different properties, the ability to decellularize tissue is different. As the degree of decellularization is different, the product must be different, as clearly shown in Figure 10. The different properties of the compounds used in Tanagho and the present invention result in different components being removed from that tissue; thus, the product of Tanagho does not maintain the same composition as the product of the present invention as it does not have the same internal structures and extracellular matrix (ECM) components as the present invention and cannot be identical. Therefore, the product in Tanagho and the product of the present invention are different, made by different process and possess different characteristics.

The process of the present invention imparts distinctive structural characteristics to the final product. Applicants respectfully submit that the Tanagho fails to meet the standard of 35 U.S.C. § 102(e). As such Tanagho does not anticipate any of the claims of the present invention. Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §102(e).

***Claim Rejections – Claims 15-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by Atala.***

The Action rejects claims 15-19 under 35 U.S.C. § 102(e) as anticipated by Atala, United States Patent Number 6,376,244 (“Atala”), which is said to disclose the claimed invention. Applicants respectfully submit that the cited reference fails to meet the standard of 35 U.S.C. § 102(e).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979). The product of claim 15-19 can be defined by the process steps by which the product is made and the process steps impart distinctive structural characteristics to the final product.

Atala relates to an organ or part of an organ, not a tissue as does the present invention. The process steps of the present invention and Atala are different and as a result the products defined by the processes are different. Even if Atala did relate to a tissue (which it does not), the process steps of Atala and the present invention are different and as a result, the products defined by the processes are different. Atala discloses a product that is made using a magnetic stir plate and a paddle or a rotator platform. The isolated organ is placed in a container with a suitable volume of fluid and stirred on the magnetic stir plate at a suitable speed. The present invention provides a tissue replacement product obtained by a soaking an obtained tissue replacement in a solution having one or more sulfobetaines, washing the tissue

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replacement in one or more solutions of a buffered salt, extracting with an anionic surface-active detergent and washing the tissue replacement in one or more solutions of a buffered salt. The process used in Atala and the present invention are clearly different and impart different characteristics on the respective products. These distinctly different processes result in distinctly different final products.

Therefore, the process of the present invention imparts distinctive structural characteristics to the final product. Applicants respectfully submit that the Atala fails to meet the standard of 35 U.S.C. § 102(e). As such Atala does not anticipate any of the claims of the present invention. Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(e).

***Claims 1-3, 9-14 and 17 are rejected under 35 U.S.C. § 103 as being unpatentable over Livesey in view of "Detergent properties and Applications"***

Applicants respectfully submit that claims 1-3, 9-14 and 17 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103(a) for the reasons stated below.

In order to establish a prima facie case of obviousness, three criteria must be met: (1) the prior art or combined references must teach or suggest all the claim limitations, (2) there must be a reasonable expectation of success, and (3) there must be some suggestion or motivation in the prior art to modify the reference or to combine reference teachings as proposed. MPEP § 2143; *In re Vacek*, 947 F.2d 488 (Fed. Cir. 1991). "The prior art must suggest the desirability of the claimed invention." MPEP § 2143.01. Both the invention and the prior art references must be considered as a whole. MPEP § 2141.02. Applicants respectfully submit that claims 1-3, 9-14 and 17 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103(a) for the reasons stated below.

A prima facie case of obviousness has not been established as (1) the prior art or combined references does not teach or suggest all the claim limitations, (2) there is no reasonable expectation of success and (3) there is no suggestion or motivation in the prior art to modify the reference or to combine reference teachings as proposed.

Livesey as discussed, *supra* (arguments incorporated herein by reference) does not include each and every limitation of the present invention. In addition, there is no reasonable expectation of success and no suggestion or motivation in the prior art as to which detergents will be optimal at removing cellular material, while preserving extracellular material. For example, studies have compared CHAPS to SB-10 and SB-16, as well as numerous other detergents, covering the zwitterionic, anionic, cationic, and non-ionic categories and significant differences were seen in their affect on nerve tissue. Claiming that all zwitterionic detergents are interchangeable is no more true than claiming that citric and hydrochloric acid are interchangeable just because they are both acids. Detergents within the same category possess

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different charge strengths, tail lengths, chain flexibility, and other characteristics. Knowing how each of these factors will impact the various components within nerve tissue (e.g., myelin, axons, collagen, laminin) is by no means obvious or trivial.

The Action specifically claims that the use of Triton X-200 versus SDS would have been a typical decision by one in the art just because Triton X-200 is gentler than SDS. Literally thousands of detergents are gentler than SDS, but the vast majority of them would not have been successful in this task of creating an acellular tissue replacement that both retains its extracellular structure and does not elicit an immune response required significant investigation and was deemed novel enough by peers in the field to deserve publication. As shown in Figures 9 and 10, the present invention appears and functions differently from the present invention.

In addition, the Action states that the use of de-ionized distilled water would have been obvious are incorrect. Livesey taught the use of de-ionized water to wash off the fascia. In contrast, distilled water loosens the myelin sheaths that surround the axons as myelin is 90% lipid and swells in the presence of distilled water and allows the subsequent detergent solutions to penetrate and disrupt the cellular membranes of the myelin sheaths.

Accordingly, Applicants respectfully submit that claim 1-3, 9-14 and 17, are not obvious over Livesey and Sigma-Aldrich and are, therefore, allowable under 35 U.S.C. § 103(a). Applicants respectfully request that the rejection of claim 13 and 23-26 be withdrawn.

***Claim Rejections – Claims 4, 7 and 18 are rejected under 35 U.S.C. § 103 as being unpatentable over Livesey in view of Atala***

Applicants respectfully submit that claims 4, 7 and 18 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103(a) for the reasons stated below.

A prima facie case of obviousness has not been established as (1) the prior art or combined references does not teach or suggest all the claim limitations, (2) there is no reasonable expectation of success and (3) there is no suggestion or motivation in the prior art to modify the reference or to combine reference teachings as proposed.



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### Conclusion

In light of the remarks and arguments presented above, Applicants respectfully submit that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending claims 1-4, 7 and 9-19 are therefore respectfully requested.

Applicants believe no fees are due at this time. If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: June 7, 2006.

Respectfully submitted,



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